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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BADIO, BARBARA P	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 09/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/741,929	AHLEM ET AL.	
	Examiner	Art Unit	
	Barbara P. Badio, Ph.D.	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10 and 23-31* is/are pending in the application.

4a) Of the above claim(s) *1-10,23,24 and 29-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/05;7/12(27)/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

First Office Action on the Merits

Election/Restrictions

1. The examiner notes the error in the definition of exemplary groups recited in paragraph 5 of the previous Office Action. For clarification of the record, the restriction requirement is restated below:

2. The Markush group set forth in the claims includes both independent and distinct inventions, and patentably distinct compounds (or species) within each invention. Each of these inventions contains a plurality of patentably distinct compounds, far too numerous to list individually. For these reasons, restriction to one of the following Groups is required under 35 U.S.C. 121, wherein a Group is a set patentably distinct inventions of a broad statutory category (e.g., Compounds, Methods of Use, etc.):

I. Claims 1-10 and 29--31, drawn to compounds and pharmaceutical compositions comprising androstane derivatives, classified in class 514, numerous subclasses.

II. Claims 23-28, drawn to various methods of use (treating/preventing osteoporosis or bone fracture), classified in class 514, numerous subclasses.

3. In addition to an election of one of Invention Sets I and II above, restriction is further required under 35 USC 121 as follows:

4. If Group II is elected, then election of one the following methods of use is required:

A. Method of treating osteoporosis

B. Method of treating bone fracture

5. In accordance with the decisions in ***In re Harnisch***, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and Ex ***parte Hozumi***, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984), restriction of a Markush group is proper where the compounds within the group either (1) do not share a common utility, or (2) do not share a substantial structural feature disclosed as being essential to that utility. In addition, a Markush group may encompass a plurality of independent and distinct inventions where two or more members are so unrelated and diverse that a prior art reference anticipating the claim with respect to one of the members would not render the other member(s) obvious under 35 U.S.C. 103.

6. With the election of any one of Groups I-III, an election of a single compound (or set of compounds) is further required including an exact definition of each substitution on the base molecule, wherein a single member at each substituent group or moiety is selected. For example, if a base molecule has a substituent group R1, wherein R1 is recited to be any one of H, OH, COOH, aryl, alkoxy, halogen, amino, etc., then applicant must select a single substituent of R1, for example OH or aryl, and each subsequent variable position. In the instant case, upon election of a single compound (or set of compounds), the Office will review the claims and disclosure to determine the scope of the independent invention encompassing the elected compound (compounds which are

so similar thereto as to be within the same inventive concept and reduction to practice). The scope of an independent invention will encompass all compounds within the scope of the claim that fall into the same class and subclass as the elected compound (or set of compounds), but may also include additional compounds, which fall in related subclasses. Examination will then proceed on the elected compound AND the entire scope of the invention encompassing the elected compound as defined by common classification. A clear statement of the examined invention, defined by those class(es) and subclass(es) will be set forth in the first action on the merits. Note that the restriction requirement will not be made final until such time as applicant is informed of the full scope of compounds along with process of using said compound under examination. This will be set forth by reference to specific class(es) and subclass(es) examined. Should applicant traverse on the ground that the compounds are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the compounds to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C 103(a) of the other.

All compounds falling outside the class(es) and subclass(es) of the selected compound and any other subclass encompassed by the election above will be directed to nonelected subject matter and will be withdrawn from consideration under 35 U.S.C. 121 and 37 C.F.R. 1.142(b). Applicant may reserve the right to file divisional

applications on the remaining subject matter. The provisions of 35 U.S.C. 121 apply with regard to double patenting covering divisional applications.

Applicant is reminded that upon cancellation of claims to a non-elected invention, the inventors must be amended in compliance with 37C.F.R. 1.48(b) if one of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 C.F.R. 1.48(b) and by the fee required under 37CFR 1.17(i).

7. If desired upon election of a single compound, applicants can review the claims and disclosure to determine the scope of the invention and can **set forth** a group of compounds, which are so similar within the same inventive concept and reduction to practice. Markush claims must be provided with support in the disclosure for each member of the Markush group. See MPEP 608.01(p). Applicant should exercise caution in making a selection of a single member for each substituent group on the base molecule to be consistent with the written description.

The following groups are exemplary:

Group I. Claims 1-10 and 29-31, drawn to a product as defined by claim 29 wherein R^9 is $-CHR^{10}-$.

Group II. Claim 29, drawn to a product as defined by claim 29 wherein R^9 is –O-.

Group III. Claim 29, drawn to a product as defined by claim 29 wherein R^9 is –S-.

Group IV. Claim 29, drawn to a product as defined by claim 29 wherein R^9 is –NR^{PR} -.

Group V. Claim 29, drawn to a product as defined by claim 29 wherein R^9 is absent.

Rationale Establishing Patentable Distinctiveness Within Each Group

8. Each Invention Set listed above is directed to or involves compounds and the use of compounds which are recognized in the art as being distinct from one another because of their diverse chemical structure, their different chemical properties, modes of action, different effects and reactive conditions (MPEP 806.04, MPEP 808.01). Additionally, the level of skill in the art is not such that one invention would be obvious over either of the other inventions, i.e. they are patentable over each other. Chemical structures that are similar are presumed to function similarly, whereas chemical structures that are not similar are not presumed to function similarly. The presumption even for similar chemical structures though is not irrefutable, but may be overcome by scientific reasoning or evidence showing that the structure of the prior art would not have been expected to function as the structure of the claimed invention. Note that in accordance with the holdings of Application of Papesch, 50 CCPA 1084, 315 F.2d 381, 137 USPQ 43 (CCPA 1963) and In re Lalu, 223 USPQ 1257 (Fed. Cir. 1984), chemical structures are patentably distinct where the structures are either not structurally similar, or the prior art fails to suggest a function of a claimed compound would have been expected from a similar structure.

The above Groups represent general areas wherein the inventions are independent and distinct, each from the other because of the following reasons:

Groups I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using the product (MPEP 806.05(h)). In the instant case, the process for using the product as claimed can be practiced with another materially different product (see the claimed compounds wherein R^9 is $-CHR^{10}-$ or –O- or –S-, etc.).

Each of the different methods of use inventions set forth in Group II is unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP sec 806.04, MPEP sec 808.01). Methods of use are unrelated if one of three differences are found between them. These differences are 1) the population being treated, 2) the material being used, and 3) the methodology for treatment. If any one or more of these differences exist and are patentably distinct, then the methods are unrelated. In the instant case, the different methods of use inventions are unrelated because the patient population treated for each method is divergent. For example, a method of treating osteoporosis presumes that the patients being treated have osteoporosis, while a method of treating bone fracture presumes the patient has a bone fracture.

In addition, because of the plethora of subclasses in each of the Group, a serious burden is imposed on the examiner to perform a complete search of the defined areas. Therefore, because of the reasons given above, the restriction set forth is proper and not to restrict would impose a serious burden in the examination of this application.

Advisory of Rejoinder

9. The following is a recitation of M.P.E.P. §821.04, Rejoinder:

> Where product and process claims drawn to independent and distinct inventions are presented in the same application, applicant may be called upon under 35 U.S.C. 121 to elect claims to either the product or process. See MPEP § 806.05(f) and § 806.05(h). The claims to the nonelected invention will be withdrawn from further consideration under 37 CFR 1.142. See MPEP § 809.02© and § 821 through § 821.03. However, if applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims, which depend from or otherwise include all the limitations of the allowable product claim will be rejoined.
>
> Where product and process claims are presented in a single application and that application qualifies under the transitional restriction practice pursuant to 37 CFR 1.129(b), applicant may either (1) elect the invention to be searched and examined and pay the fee set forth in 37 CFR 1.17(s) and have the additional inventions searched and examined under 37 CFR 1.129(b)(2), or (2) elect the invention to be searched and examined and not pay the additional fee (37 CFR 1.129(b)(3)). Where no additional fee is paid, if the elected invention is directed to the product and the claims directed to the product are subsequently found patentable, process claims which either depend from or include all the limitations of the allowable product will be rejoined . If applicant chooses to pay the fees to have the additional inventions searched and examined pursuant to 37 CFR 1.129(b)(2), even if the product is found allowable, applicant would not be entitled to a refund of the fees paid under 37 CFR 1.129(b) by arguing that the process claims could have been rejoined. 37 CFR 1.26 states that "[m]oney paid by actual mistake or in excess will be refunded, but a mere change of purpose after the payment of money...will not entitle a party to demand such a return..." The fees paid under 37 CFR 1.129(b) were not paid by actual mistake nor paid in excess, therefore, applicant would not be entitled to a refund.
>
> In the event of rejoinder, the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104 - 1.106. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the

> requirements of 35 U.S.C. 101, 102, 103, and 112. If the application containing the rejoined claims is not in condition for allowance, the subsequent Office action may be made final, or, if the application was already under final rejection, the next Office action may be an advisory action.

The following is a recitation from paragraph five, "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. §103(b)" (1184 TMOG 86(March 26, 1996)):

> "However, in the case of an elected product claim, rejoinder will be permitted when a product claim is found allowable and the withdrawn process claim **depends from or otherwise includes all the limitations of** an allowed product claim. Withdrawn process claims not commensurate in scope with an allowed product claim will not be rejoined." (emphasis added)

Therefore, in accordance with M.P.E.P. §821.04 and In re Ochiai, 71 F.3d 1565, 37 USPQ 1127 (Fed. Cir. 1995), rejoinder of product claims with process claims commensurate in scope with the allowed product claims will occur following a finding that the product claims are allowable. Until, such time, a restriction between product claims and process claims is deemed proper. Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution to maintain either dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

10. Applicant's election with traverse of the subject matter of claim 28 in the reply filed on June 10, 2005 is acknowledged. The traversal is on the ground(s) that the scope of the claimed invention is reduced and, thus, more easily searched. According to applicant, the subject matter of claim 29 should be treated as a single invention for the examination. The examiner assumes applicant meant "claim 23" since the elected

compound is not encompassed by claim 29, i.e., R^3 is not H. This is not found persuasive because the compounds encompassed by claim 23 fall within several different classes because of the definition of "R^9". Therefore, a search of the entire scope of claim 23 would require several different search strategies that would impose a burden on the examiner.

11. Based on applicant's election of the subject matter of claim 28, the following generic group will be examined in the present application. The treatment of osteoporosis utilizing compounds as defined by claim 23 wherein R^9 is –CHR^{10}-.

12. Claims 1-10, 23, 24 and 29-31 stand withdrawn from further consideration as being drawn to a nonelected invention. Claims 25-28 will be examined to the extent they read on the generic group defined in #11 accordance with MPEP § 803.02. Note: Claims 23 and 24 do not encompass the elected species because R^{10} as defined by claim 23 is not H.

Double Patenting

13. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double

patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

14. Claims 25-28 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim1-10, 15-19, 22 and 23 of copending Application No. 10/877,911. Although the conflicting claims are not identical, they are not patentably distinct from each other because they both encompass a method of treating osteoporosis utilizing the claimed compounds. Unlike the copending Application, the present Application recites a limited genus of compounds. However, there is an overlap in the compounds recited by the two inventions. For example, both encompass applicant's elected compound, i.e., 3α,17β-dihydroxy-19-norandrost-4-ene (see claim 28 of the present Application and claim 19, 4th compound of the copending Application) and, thus, the utilization of the elected compound in the treatment of osteoporosis would be obvious to the skilled artisan based on the disclosure of the cited copending Application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

15. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

16. Claims 25-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are (1) the nature of the invention, (2) the breadth of the claims, (3) the state of the prior art, (4) the predictability or unpredictability of the art, (5) the amount of guidance or direction presented, (6) the presence or absence of working examples, (7) the relative skill in the art and (8) the quantity of experimentation necessary. When the above factors are taken into consideration, the examiner's position is that one skilled in the art could not perform the invention commensurate in scope with the instant claim without undue experimentation.

The instant claim contemplates the use of the claimed compounds in the prevention of osteoporosis. However, the present specification lacks guidance and/or working examples of the prevention of osteoporosis. The present specification also lacks descriptive of how the skilled artisan would determine a person susceptible to osteoporosis and, thus, in need of preventive treatment. Thus, in order to practice the claimed invention commensurate in scope with the instant claims, the skilled artisan

would have to search the prior art to find, if possible, a model for determining a person prone to osteoporosis and, thus, in need of preventive treatment. The amount of experimentation necessary to make said determination is undue because of the lack of guidance and/or working example in the present specification.

Claim Objections

17. Claims 25-28 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

The instant claims recite compounds wherein R^9 is $-CH_2-$. Parent claim 23 recites R^9 is $-CHR^{10}-$. However, the definition of R^{10} does not include a hydrogen atom.

Claim Rejections - 35 USC § 102

18. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

19. Claims 23-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Kousteni et al.

Kousteni et al. teach a reversal of bone loss in mice utilizing a synthetic estrogen ligand, 3α,17β-dihydroxy-19-norandrost-4-ene (see the entire article, especially Abstract; page 845, paragraph 4). The method of use taught by the reference is encompassed by the instant claims.

Claim Rejections - 35 USC § 103

20. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

21. Claims 25-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kousteni et al.

Kousteni et al. teach a reversal of bone loss in mice utilizing a synthetic estrogen ligand, 3α,17β-dihydroxy-19-norandrost-4-ene (see the entire article, especially Abstract; page 845, paragraph 4).

The instant claims differ from the reference by reciting the treatment of osteoporosis. However, the art teaches (a) a reduction in bone mass is the underlining cause of osteoporosis (see Stedman's Medical Dictionary) and (b) the use of estrogen replacement therapy in treatment of bone loss/osteoporosis (see for example page 845, paragraph 5 of the cited reference). Therefore, the skilled artisan in the art would be motivated to utilize 3α,17β-dihydroxy-19-norandrost-4-ene in the treatment of

osteoporosis because of the teachings by Kousteni that the compound reverses bone loss and increases bone mass and strength.

Other Matters

22. No support was found for the utilization of the claimed compound in the treatment of osteoporosis in applicant's prior applications.

Telephone Inquiry

23. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Barbara P. Badio, Ph.D. whose telephone number is 571-272-0609. The examiner can normally be reached on M-F from 6:30am-4:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Barbara P. Badio, Ph.D.
Primary Examiner
Art Unit 1617

BB
September 13, 2005